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Association of dietary fiber and depression symptom: A systematic review and meta-analysis of observational studies

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ABSTRACT

Background: A potential relationship between depression and the intake of dietary fiber has been hypothesized in several studies. However, no meta-analysis has been conducted so far to explore the association between these two variables. Hence, we designed the present meta-analysis to elucidate the relationship between the intake of dietary fiber and depression.

Methods: A comprehensive search was performed using the PubMed/Medline, Scopus, Web of Science and Google Scholar databases to identify any relevant studies published from inception to October 2019. Observational studies (cross-sectional and case-control) were included in the analysis.

Results: Pooled analysis from the random-effects model of four case-control studies revealed that the consumption of dietary fiber in patients with depression was significantly lower *versus* healthy controls (WMD: -1.41 mg/dl, 95 % CI: −2.32, −0.51, P = 0.002). No significant heterogeneity was demonstrated among the analyzed studies (I^2 = 4.0 %, P = 0.37). By pooling 5 effect sizes of cross-sectional studies (with a total of 97,023 subjects), we demonstrated that a higher dietary consumption of fiber was associated with significantly lower odds of depression (OR = 0.76; 95 % CI: 0.64, 0.90; P = 0.010), with a low heterogeneity seen among the retrieved studies (I^2 = 43.9 %; P = 0.12).

Conclusion: An increased intake of total dietary fiber is associated with lower odds of depression. Further studies are needed to evaluate the relationship between the different types of dietary fiber and depression.

1. Introduction

Depression and anxiety are common psychiatric disorders which have become significant threats to public health worldwide.[1] Depression is a frequently encountered mental disorder that affects globally more than 264 million people of all ages. It is a leading cause of disability worldwide and is a major contributor to the overall global burden of disease. Women seem to be more particularly affected by depression *versus* men. Depression can cause the affected person to suffer greatly and function poorly at work or at school and can even affect one's family. At its worst, depression can lead to suicide.[2] The burden of depression and other mental health conditions has been on the rise globally, with depressive disorder becoming one of the top leading causes of years lived with disability (YLDs) in 2017 for both sexes

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combined.[3]

Depression continues to be the leading cause of disability worldwide and, according to recent predictions, it will emerge as the principal cause of disease burden by 2030.[4] Furthermore, mental health disorders also have consequences on a nation's economy[5] and it is, thus, necessary to identify potentially modifiable risk factors for depression and other psychiatric illnesses.

A plethora of epidemiological data has shown a sizeable association between depression and several components of the diet, *e.g.* fish, fruits, vegetables, and some nutrients such as folate, zinc and iron.[6–9] More recently, a systematic review and meta-analysis documented an inverse linear relationship between the consumption of fruit and vegetables and the risk of depression.[12] Among the aforementioned articles, dietary fiber has been cited as one of the potential dietary factors influencing the progression of depressive symptoms.[10] Previous studies have highlighted noteworthy inverse associations between dietary fiber and depressive symptoms.[11,12] Increasing the dietary fiber intake in the diet has the capacity to improve the cognitive function of the elderly.[13] Late-life depression is often accompanied by cognitive impairment. Depression, cognitive impairment and dementia are all common in older adults and the relationship between them is bidirectional and complex.[14] Based on the potential evidence of the efficacy of dietary fiber on reducing the risk of depression in humans, it is crucial to synopsize and appraise the quality of the existing data. Hence, the purpose of the present systematic review and meta-analysis of published observational studies was to evaluate the relationship between the intake of dietary fiber and depression.

2. Methods

2.1. Search strategy

A predetermined search strategy was implemented until October 2019 using the Web of Science, PubMed/Medline, Scopus and Google Scholar databases. The study selection was performed by two researchers independently. Keywords from the medical subject headings (Mesh) database were used for this search as follows: (food OR diet OR dietary' OR nutrition OR vegan OR diet consumption) AND (fiber OR polysaccharide OR brans wheat OR soluble fiber OR insoluble fiber OR roughage OR dietary fiber) AND (depression OR mood disorder OR mental disorder OR major depression OR depression emotional OR depressive symptoms).

2.2. Study selection

We considered the participant, intervention, comparison, outcome, time, and study design (PICOTS) criteria to ascertain the study inclusion criteria. We included observational studies that examined the association between depressive symptoms and the intake of dietary fiber. After excluding the duplicate articles, two authors independently reviewed the titles, abstracts or full-texts of the retrieved papers to detect potentially relevant manuscripts. Finally, original studies were included in the present meta-analysis if they have met the following inclusion criteria - (i) population: adults and children of all ages and genders; (ii) intervention/exposure: dietary fiber intake; (iii) comparison: quantity of dietary fiber ingestion; (iv) outcome: depression; and (v) study design: cross-sectional, case-control or cohort studies.

Articles were excluded from the analysis if they were - (i) studies not reporting dietary fiber type and quantity, not reporting depression score using validated tools and not estimating the association between dietary fiber intake across groups with and without depression, (ii) reviews, editorials, letters, commentaries or grey literature, (iii) unpublished studies, (iv) conference proceedings (v) duplicates or irrelevant studies, and (vi) animal, or *in vitro* or *in vivo* studies.

2.3. Data extraction

Two independent researchers reviewed the data and an additional reviewer resolved any disagreements. We extracted vital information from the eligible studies, i.e.: (i) first author, (ii) year of publication, (iii) country where the trial was performed, (iv) study design, (v) sample size, (vi) patient demographics [age (age range or age mean, SD), gender], (vii) type of fiber, (viii) amount of fiber intake (mg/day), (ix) outcome and outcome assessment tool and, lastly, (x) exposure and exposure assessment tool and adjusted variables. Additionally, pertinent effect sizes [odds ratio (OR), risk ratio (RR), hazard ratio (HR), mean intake (standard deviation, SD) and regression or correlation coefficients], their corresponding 95 % confidence intervals (CI), in addition to adjusted covariates, were extracted from these papers.

2.4. Quality assessment

The methodological quality of the eligible studies was appraised using the ROBINS-1 (formerly called A Cochrane Risk of Bias Assessment Tool) for Assessing the Quality of Nonrandomized cross-sectional and case-control Studies in Meta-Analysis.[15] ROBINS-I provides seven bias domains. The judgments within each domain carry forward to an overall risk of bias judgment for the outcome being assessed. These seven bias domains covering confounding, selection of participants into the study, measurement of interventions, deviations from intended interventions, missing data, measurement of outcomes and selection of reported results. The categories for risk of bias judgments are "Low risk", "Moderate risk", "Serious risk" and "Critical risk" of bias. Low risk shows that the study is comparable to a well-performed randomized trial, Moderate risk of bias indicates that the study provides sound evidence for a non-randomized study but cannot be considered comparable to a well performed randomized trial. Serious risk of bias indicates the study has some important problems. Critical risk of bias shows that the study is too problematic to provide any useful evidence and should not be included in any synthesis. No information indicates that there is no information on which to base a judgment about risk of bias.

2.5. Statistical analysis

All statistical analyses were performed using STATA v12.0 (Stata Corp, College Station, TX, USA) software. Data were combined and if there were $\geq$3 case-controls, the random effects model was used and reported as weighted mean differences (WMDs). To estimate the association between dietary fiber and depression, the odds ratio (OR) and their corresponding 95 % confidence interval (CI), the log OR and its standard error (SE) were calculated. A random-effects model was used to compute the pooled effect size in view of anticipated heterogeneity. Between-study heterogeneity was determined using the Higgins I^2 statistic.[16] I^2 values of <25, 25–50 and >50 % were designated as low, moderate and high heterogeneity respectively.[17]. When significant heterogeneity was detected, subgroup analyses were performed to identify the principal sources of heterogeneity. A sensitivity analysis was applied to assess the contribution of each study to the overall mean difference. Publication bias was evaluated by visual inspection for asymmetry of funnel plot and validated by the Egger's linear regression statistic, and P-values <0.05 were considered statistically significant unless stated otherwise.[18]

3. Results

3.1. Study selection

Following the initial database search, 2569 publications remained after the removal of duplicate papers. Subsequently, 2468 publications were eliminated based on the title and abstract screening, yielding 101 publications for the full-text review. Ultimately, 9 articles were included

in the meta-analysis (Fig. 1).

3.2. Characteristics of the included studies

The general characteristics of the incorporated publications are presented in Table 1. Among the studies integrated in this systematic review that have been published up to October 2019, 4 studies had a case-control design[19–22] and 5 studies had a cross-sectional design.[11,12,23–25] All the studies incorporated both genders, except for one paper which exclusively analyzed women.[25] The total sample size was 97,023 in the cross-sectional studies and 673 patients in the case-control cohorts.

The dietary fiber consumption and its impact on depression odds was considered in all the eligible cross-sectional studies. In addition, the mean (SD) intake of dietary fiber were reported in all case-control studies. The diagnosis of depression was based on a variety of assessment tools including self-report inventories and clinician-rated scales with some studies using more than one: three studies used the Center for Epidemiological Studies-Depression Scale (CES-D),[12,22,23] three studies used the Geriatric Depression Scale (GDS),[19,20,24] one study used the Hospital Anxiety and Depression Scale (HAD),[21] two studies used the Patient Health Questionnaire (PHQ),[11,21] one study used Mental Health Index (MHI)[23] and one study used the Burnam 8-item scale (includes 2 items from the Diagnostic Interview Schedule and 6 items from the Center for Epidemiologic Studies–Depression Scale).[25] The intake of dietary fiber was assessed *via* the following questionnaires: four studies used the Food Frequency Questionnaire (FFQ),[21,23–25] four studies used the 24 h dietary recall,[11,19,20,22] and one study used the Brief Self-Administered Diet History Questionnaire (BDHQ).[12] The methodological quality of the eligible studies was appraised using the ROBINS-1. Three of the studies had low risk of bias,[12,19,26] two studies had a moderate risk of bias,[11,25] and four studies had a serious risk of bias,[20,21,24,27] (Supplementary Table 1)

3.3. Meta-analysis results for case-control studies

Pooled analysis using the random-effects model of the 4 case-control studies revealed that the consumption of dietary fiber in participants with depression was significantly lower than in controls (WMD: −1.41 mg/dl, 95 % CI: −2.32, −0.51, P = 0.002) without a significant heterogeneity seen among the papers (I^2 = 4.0 %, P = 0.37) (Fig. 2).

3.4. Meta-analysis results for cross sectional studies

Pooled analysis using the random-effects model of 5 effect sizes of cross-sectional studies with a total of 97,023 people determined that a higher dietary fiber consumption was associated with significantly lower odds of depression (OR = 0.76; 95 % CI: 0.64, 0.90; P = 0.010), with a low heterogeneity demonstrated among the studies (I^2 = 43.9 %; P = 0.12) (Fig. 3).

3.5. Results of sensitivity analysis and publication bias

To perform a sensitivity analysis to appraise the impact of each individual study on the computed pooled effect size, a stepwise removal of one study at a time was conducted that observed no significant effect of any individual study on the pooled effect sizes (Supplementary Fig. 1). The judgment of the publication bias by the visual review of the funnel

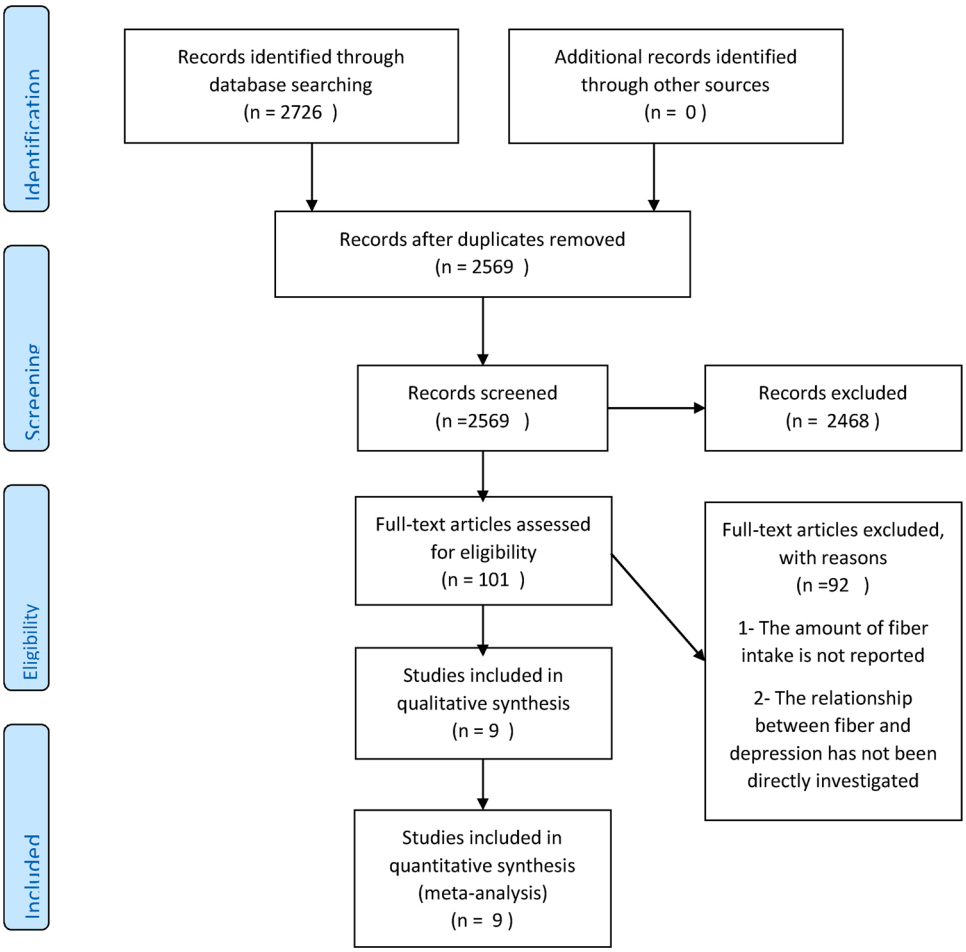

Fig. 1. The flow diagram of study selection.

Table 1
Included Study Characteristics by Population.

First Author (Year)	Study Design	Country	Age Rangey	Gender M/F	Sample Size	Type of Fiber	Instrument of Outcome	Exposure/ Comparisong/ day	Exposure Assessment	Adjustments	Quality
Gougeon et al., 2017[19]	Case-Control	Canada	67−83	M&F	316	Total Fiber	GDS >11/ Antidepressants	20·1/19·9	3 × 24-Hour Dietary Recall	Physical Activity, Functional Autonomy and Stressful Life	low
Guligowska et al., 2016[20]	Case-Control	Poland	≥60	M&F	130	Total Fiber	International Classification of Diseases 10th revision criteria	17.85/20.01	24-Hour Dietary Recall	Not reported	serious
Othman et al., 2018[21]	Case-Control	Tunisia	≥18	M&F	100	Total Fiber	HAD / PHQ-9	13.43/16.57	FFQ Food Photography Manual	Not reported	serious
Park et al., 2010[22]	Case-control	Korea	≥20	F	130	Total Fiber	CES-D20 ≥ 16	12.1/13.5	3-Day Dietary Recall	Not Reported	serious
Miki et al., 2015[12]	Cross-Sectional	Japan	19–69	M&F	1977	Total Fiber	CES-D20 ≥ 16	4.0/7.6 gr/ 1000 kcal	BDHQ	Age, Sex, Marital Status (Married or Other); Job Grade (Low, Middle or High); Night Or Rotating Shift Work (Yes/ No);Overtime Work, Job Strain Physical Activity, Leisure-Time Physical Activity, Sleep Duration, Smoking, Alcohol Drinking, Body Mass Index, Vitamin B12, Intake of Folate, Total Energy Intake, N-3 Polyunsaturated Fatty Acids, Magnesium, Zinc, Serum 25-Hydroxy-vitamin D Concentrations	low
Xu et al., 2018[11]	Cross-Sectional	US	≥20 years	M&F	16807	Total Fiber	PHQ ≥10	12.7/15.2	2 × 24-Hour Dietary Recalls	Total Energy Intake, Smoking Status, Alcohol Consumption, Work Physical Activity	moderate
Gopinath et al., 2016[26]	Cross-Sectional	Australia	≥55 years	M&F	2334	Total Fiber	CES-D10 ≥ 10/ MHI ≤ 59 Antidepressant Use	≤21·1/≥27·6	FFQ	Energy, Age, Sex, Cognitive Impairment (Mini-Mental State Exam <24), Walking Disability, Receiving Pension, Antidepressant Use, Previous History of Stroke And Arthritis.	low
Woo et al., 2006 [24]	Cross-Sectional	Hong Kong,	≥65 years	M&F	3999	Total Fiber	GDS ≥ 8	0-6 / ≥13	7-Day FFQ	Total Calorie Intake, Age, Gender, Education Level, Socioeconomic Status, And Number Medical Diseases (History of Stroke, Myocardial Infarction, Angina, Congested Heart Failure, Or Diabetes Mellitus	serious
Gangwisch et al., 2015[25]	Cross-Sectional	US	50−79	F	69954	Total Fiber	Burnam 8-item scale	10.719/ 21.136	FFQ 4-d food record four 24-h dietary recalls	nutrient density race-ethnicity, education, income, BMI, diabetes, hypertension, hormone replacement therapy, stroke, myocardial	moderate

(*continued on next page*)

Table 1 (*continued*)

First Author (Year)	Study Design	Country	Age Rangey	Gender M/F	Sample Size	Type of Fiber	Instrument of Outcome	Exposure/ Comparisong/ day	Exposure Assessment	Adjustments	Quality
										infarction, Alzheimer disease, cardiovascular disease, cancer, physical activity, stressful life events, social support, smoking, alcohol, and energy-adjusted intakes of SFAs, MUFAs, PUFAs, and trans fatty acids	

Abbreviations & Acronyms: F, Female; M, Male; Center for Epidemiological Studies-Depression Scale (CES-D10); Center for Epidemiological Studies-Depression Scale (CES-D20); Geriatric Depression Scale (GDS); Hospital Anxiety and Depression Scale (HAD); Mental Health Index (MHI); Patient Health Questionnaire (PHQ); Food Frequency Questionnaire (FFQ); Brief Self-Administered Diet History Questionnaire (BDHQ).

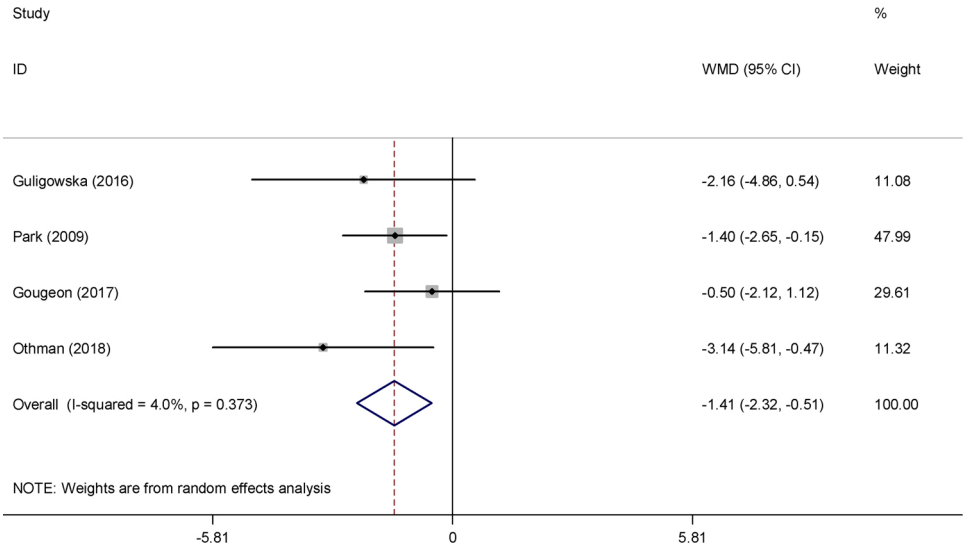

Fig. 2. Pooled results of case-control studies for the analysis of dietary fiber intake in humans with depression. This figure revealed that the consumption of dietary fiber in participants with depression were significantly lower than control groups.

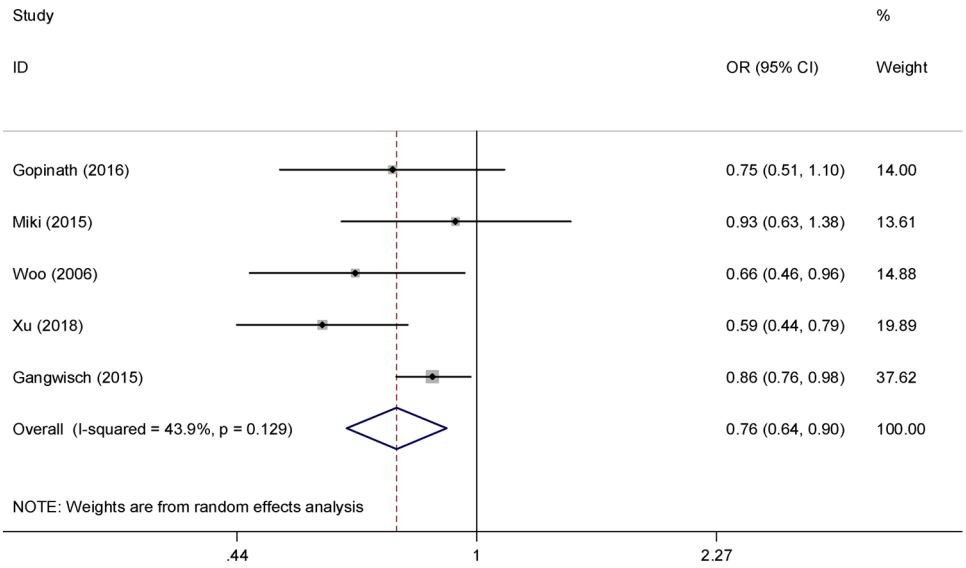

Fig. 3. Forest plot of association between dietary fiber intake and odds of depression in cross sectional studies. This figure determined that higher dietary fiber consumption was associated with significantly lower odds of depression.

plot was difficult due to the limited number of studies (Supplementary Fig. 2). However, the Egger's test also showed no evidence of bias for case-control (P = 0.35) or cross-sectional studies (P = 0.31).

4. Discussion

The findings from this systematic review and meta-analysis discerned that the consumption of dietary fiber in participants with depression was significantly lower compared to the control groups in 4 case-control studies[19–22] Moreover, a higher dietary fiber ingestion was associated with significantly lower odds of depression in 5 cross-sectional studies.[11,12,23–25] The majority of participants in the analyzed studies were adults, including elderly subjects.

The conclusions of our research are also endorsed by the findings of the Women's Health Initiative Observational Study, a large prospective cohort investigation conducted on 87,618 women, which discovered that a reduced intake of dietary fiber, fruit and vegetables was associated with increased odds of incident depression after 3-years of follow-up (P = 0.0157 and P < 0.0001 respectively).[25] Conversely, the intake of refined grains led to opposite changes: as the dietary glycemic index decreased, the odds of depression increased in the fully adjusted models. Another cross-sectional study, which failed to meet our inclusion criteria, revealed that women with fewer depressive symptoms were inclined to have higher intake of total and soluble dietary fiber, further validating our results.[10]

Our conclusion echoes a preceding cross-sectional research, the Study on the Epidemiology of Psychological-Alimentary Health and Nutrition (SEPAHAN), conducted on 3172 Iranian participants. According to the results derived from SEPAHAN, a negative association between the intermediary intake of whole grain foods and anxiety, and a positive relationship between the ingestion of refined grains and depression and anxiety in were recorded in women.[28] Moreover, an analysis of a prospective cohort of 15,546 Spanish university graduates—the *Seguimiento Universidad de Navarra* (SUN)—concluded that an increased consumption of added sugars and low-quality carbohydrates, as assessed by the carbohydrate quality index (CQI), was associated with an elevated risk of depression. CQI was defined as a high whole-grain and fiber intake, low glycemic index and the consumption of solid (instead of liquid) carbohydrates.[29,30]

Whole grains are acknowledged to contain high quantities of bioactive compounds, such as fiber, vitamin B, vitamin E, magnesium, antioxidants and phytoestrogens, which can also be found in fruits and vegetables in various proportions.[31] To the best of our knowledge, no systematic reviews and (or) meta-analyses that have investigated the correlation between the dietary intake of fiber and the risk of depression have been conducted so far. To date, only one systematic review and meta-analysis evaluated the association between the intake of fruits and vegetables and the risk of depression. The meta-regression analysis established an inverse relationship between the two variables, pointing out that for every 100-g increase in the consumption of fruits or vegetables, the risk of depression decreases by 3 % and the odds decrease by 5 %, according to findings from cohort and cross-sectional studies, respectively.[32] Accordingly, an elevated intake of fruits and vegetables was linked with an increased dietary intake of fiber. However, there was no objective evaluation or quantification of the fiber intake as part of the nutritional analysis and its direct effect on depression in the aforementioned study.[32]

Dietary fiber (soluble and insoluble) has exhibited remarkable physiological effects and has been associated with various health benefits in humans. An increased intake of dietary fiber has been said to lower the risk of cardiovascular disease and type 2 diabetes mellitus, modulate glycemic control and regulate gut health, appetite and bodyweight.[33,34] Given the limited evidence from epidemiological studies that have evaluated the relationship between dietary fiber and depression, the underlying molecular mechanisms *via* which the intake of dietary fiber modulates the risk of depression have yet to be elucidated.

Multiple theories have been proposed: changes in the composition of the intestinal microbiome,[34,35] which lead to a consequent modulation of several neurotransmitters (*e.g.* serotonin),[36] alteration of the stress-induced response,[37] mitigation of the inflammation cascade and regulation of oxidative stress.[38] Thus, we may assume that this relationship is complex and derives from the interplay between the gut, immune, neural, endocrine and metabolic pathways which ultimately modulate the function of the brain.[39] Furthermore, the fermentation of dietary fiber generates short chain fatty acids (SCFAs) *via* the intestinal microbiota, and consequently limits the contribution of inflammation in the development of depression.[34,40–43] Additionally, dietary fiber reduces the glycemic index which is extremely clinically relevant, since a high glycemic index has been associated with an increased risk of depression.[25] Lastly, dietary fiber averts postprandial hyperglycemia, thereby counteracting the generation of free radicals and inflammatory cytokines and, ultimately, limiting their interplay in the development of depression.[25]

Our study has several strengths and limitations. Perhaps the greatest strength of our research is that this is the first meta-analysis to investigate the association between the intake of dietary fiber and the odds of depression. Other strengths of our paper are the inclusion of large cumulative sample sizes and the integration in the analysis of a diverse and heterogeneous population: adults of varying ages and genders, different socioeconomic statuses, employment backgrounds, educational levels and comorbidities, and of patients with different grades of depression in terms of severity. Even if the patients originated from multiple countries, several dietary behaviors might have been omitted or might have been under-represented in our analysis, limiting the generalization of our results to other populations. As the most important limitation of this study, we could not evaluate the relationship between depression and the type of fiber consumed in the diet, because in many studies the type of dietary fiber was not documented.

Moreover, some studies analyzed depressive symptoms for a short period of time, whereas these symptoms can often be transient and reversible. Others assessed clinical depression and patients on antidepressant medication, often diagnosed with a more severe form of depression. Additionally, a variety of validated tools, including self-reported inventories *versus* clinician-rated scales for defining depression, have been used in the analyzed papers. There tools vary in terms of sensitivity, specificity, content validity, test-retest reliability and inter-rater reliability, and can influence the results of the assessment.[32,44] These reports used a great variety of validated nutritional questionnaires which were dependent on dietary recall, memory and perception of portion sizes. Thus, the participants' adherence to a certain diet could have led to a misclassification bias of the dietary components and random within-person variation because they relied on self-reporting, consequently resulting in the attenuation of any correlation.[32,44]

Although there was an adjustment for covariates in the selected studies, not all the reports performed this analysis and in others the analysis was inconsistent, potentially omitting residual confounders and thus attenuating any true association. Since we also analyzed studies with a cross-sectional design, a causal link between the intake of dietary fiber and the risk of depression cannot be established. Hence, prospective randomized-controlled trials are needed to demonstrate the causal link between the intake of dietary fiber and the risk of depression. Future studies should also assess depression carefully, taking into consideration the grade of severity and ideally using the same validated clinician-operated diagnostic tool rather than a screening tool, the same validated nutritional assessment questionnaire for all the patients and putative biomarkers to validate the self-reported dietary intake.

5. Conclusion

In conclusion, we report that that a higher intake of total dietary fiber is associated with lower risk of depression. Given that depression is acknowledged as a global public health concern which leads to

substantial societal and economical costs, further prospective studies, and in particular randomized-controlled trials, are warranted to evaluate and further explore this association. Future research papers should also assess whether changes in the content and type of the dietary fiber intake of the patients at risk for depression can serve as effective preventative strategy in the management of this mental health disorder.

Declaration of Competing Interest

The authors report no declarations of interest.

Acknowledgments

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ctim.2020.102621.

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